

To Cite:

Sagar VVSS, Acharya S, Gomase S, Singh RK, Shukla S, Kumar S, Akhil CVS. Ventricular Septal defect (VSD) as an extra renal manifestation in Congenital Anomalies of Kidney and Urinary Tract (CAKUT) Syndrome: A rare Case report. Medical Science, 2022, 26, ms41e2003.
doi: <https://doi.org/10.54905/disssi/v26i119/ms41e2003>

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Peer-Review History

Received: 24 November 2021
Reviewed & Revised: 28/November/2021 to 17/January/2022
Accepted: 19 January 2022
Published: 24 January 2022

Peer-review Method

External peer-review was done through double-blind method.

URL: <https://www.discoveryjournals.org/medicalscience>



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Ventricular Septal defect (VSD) as an extra renal manifestation in Congenital Anomalies of Kidney and Urinary Tract (CAKUT) Syndrome: A rare Case report

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ABSTRACT

Congenital abnormalities of the kidney and urinary tract (CAKUT) are a key cause of morbidity and a substantial contributor to end-stage renal disease (ESRD). These anomalies are the most prevalent form of birth malformation. Other system abnormalities such as those of the heart, gastrointestinal tract, central nervous system, skeletal system, respiratory system, facial dysmorphism, reproductive system, abdominal wall coexist with these anomalies. Congenital heart defects (CHD) are the most frequent complication in this syndrome, according to previous data. These findings show a similar genetic aetiology for congenital heart disease (CHD) and renal abnormalities, implying that CHD patients are at a significantly increased risk of renal anomaly outcomes. To avoid renal damage and chronic kidney disease, it is crucial to be aware of this linkage in the early treatment and diagnosis of CAKUT. We present a case of a 23 year old male who presented to us with symptoms of ESRD and was diagnosed to be case of CAKUT syndrome with VSD as the extra renal association.

Keywords: Congenital, CAKUT, ESRD, genetics, hypodysplasia.

1. INTRODUCTION

Congenital abnormalities of the kidney and urinary tract (CAKUT) are the most prevalent forms of birth malformation, accounting for 40–50% of paediatric and 7% of adult end-stage renal failure globally. CAKUT is responsible for 30–60% of ESRD in children (Barakat et al., 1988). CAKUT encompass a wide spectrum of anatomical distortions caused by defects in kidney and urinary tract morphogenesis. To prevent the onset of ESRD, it is

essential to detect these abnormalities and begin treatment. Concurrent CAKUT in CHD may be caused by certain genetic causes, environmental impacts on foetal development, and drugs taken during pregnancy. It is essential to comprehend the prevalence, maternal risk factors, and natural history of CAKUT correlated to CHD. CAKUT's pathogenesis is based on the malfunction of normal nephrogenesis as a result of environmental and genetic factors. Prenatal sonography is mainly used to detect CAKUT, however many instances go unnoticed until adulthood. CAKUT encompasses a wide range of diseases with varying degrees of severity and renal outcomes. Until now, categorization system that was commonly used has been based on anatomical traits. The most common phenotype reported is ureteropelvic junction obstruction. All anomalies can be unilateral or bilateral, and in case of multiple anomalies, it can be difficult to determine independent occurrence of anomalies or whether one of them is the phenotype's primummovers (Jiang et al., 2020; San Agustin, 2016).

CAKUT can sometimes manifest as an isolated feature or as part of a systemic illness with extrarenal presentations, making diagnosis and clinical categorization even more complex. About 50 to 60 percent of those who are affected have additional organ system abnormalities predominantly affecting cardiovascular system manifesting as congenital heart disease. This correlation can be attributed to similar embryological origin of renal and cardiovascular systems. Various genetic associations have also been reported supporting the above correlation.

In our case we are discussing a patient having hereditary unilateral renal hypoplasia (left side) coexisting with ventricular septal defect presented in a state of end stage renal disease. Hemodialysis was initiated and renal transplantation was planned.

2. CASE REPORT

A 23 year old male admitted with complaints of breathlessness at rest (NYHA-Grade IV), bilateral lower limb swelling, facial puffiness, easy fatiguability, reduced appetite since 2 months. Patient had no history of chest pain, abdominal pain, vomitings, loose stools, hemoptysis, and abdominal distension. Patient is not a known diabetic or hypertensive. Patient had a congenital cardiac anomaly diagnosed 12 years back for which patient had no documentation and had taken some conservative management.

On general examination patient was afebrile having heart rate 94/minute and blood pressure of 130/90mm Hg, respiratory rate of 18/minute of abdominothoracic type. Patient had pallor, pedal edema. Cardiovascular examination revealed pansystolic murmur which is of grade 3 intensity, high pitched, and best heard in left parasternal area 4th intercostal space in inspiration, systolic thrill present in pulmonary area. Respiratory system examination revealed bilateral infrascapular crackles. No abnormality noted in abdominal and central nervous system examination.

Hematological investigations revealed haemoglobin 8.3gm/dl, total leukocyte count 13300 cells/cumm, platelet count 2.96 lakhs, urea 146, creatinine 8.8, serum sodium 134meq/l, serum potassium 6.2meq/l. Arterial blood gases suggestive of severe metabolic acidosis. Ultrasound abdomen revealed normal sized right kidney with Grade III renal parenchymal disease and left kidney not visualised in renal fossa Hypoplasia (figure 1a, 1b).



Figure 1A and 1B showing normal right kidney and left empty renal fossa

As left kidney was not visualised, CT KUB was done which revealed shrunken left kidney with minimal perinephric fat stranding around right kidney (Figure 2A and B).

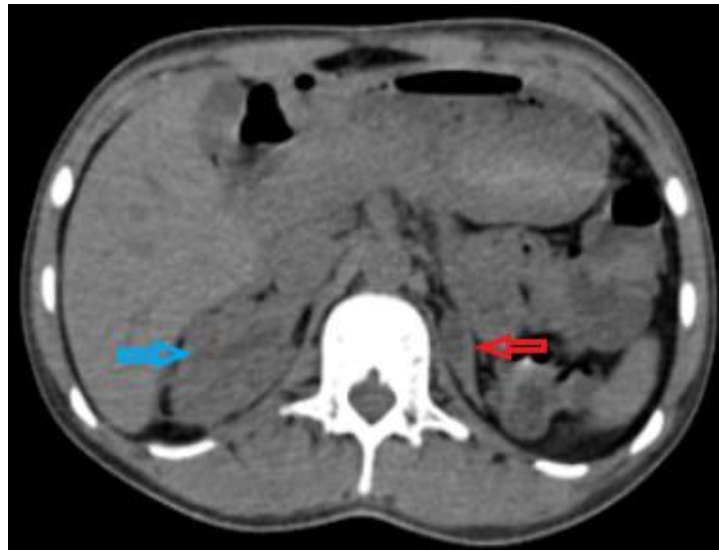


Figure 2A Non contrast axial computed tomography section showing right kidney (blue arrow) with normal oriented pelvi-calyceal axis (anteromedial) and small shrunken left kidney (red arrow) is seen in left renal fossa with perinephric fat.

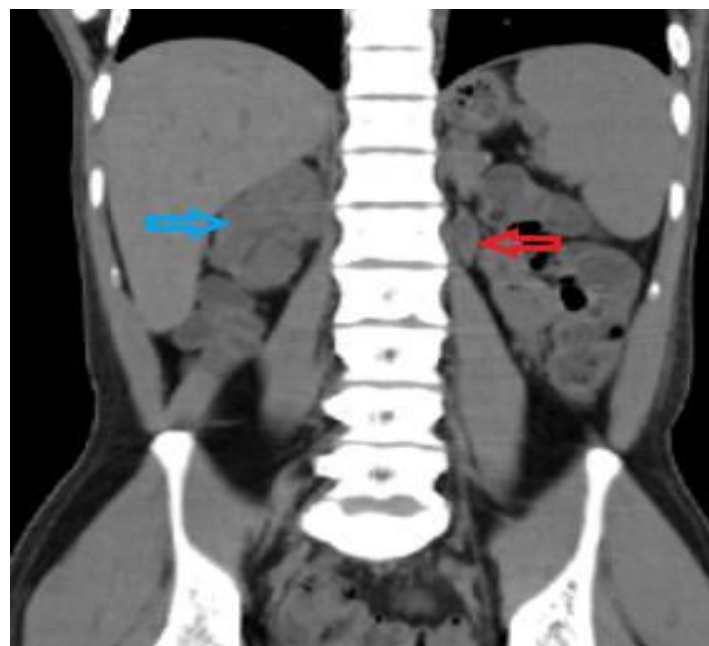


Figure 2B Non contrast coronal computed tomography section showing right kidney (blue arrow) and small shrunken left kidney (red arrow) is seen in left renal fossa.

Suspecting congenital renal anomaly, two dimensional echocardiography was done to rule out associated congenital heart disease which revealed large outlet ventricular septal defect of 13mm which is restricted by septal tricuspid leaflet/septal aneurysm giving minimum left to right shunt (low flow), mildly dilated left heart chambers, left ventricular hypertrophy present, no coarctation of aorta (Figure 3).

Hemodialysis was initiated for patient in view of signs of overload such as pulmonary edema, metabolic acidosis, refractory hyperkalemia, and uremia. Patient had been planned for renal transplantation. Patient was advised for serial echocardiography 6 monthly for ventricular septal defect followup.

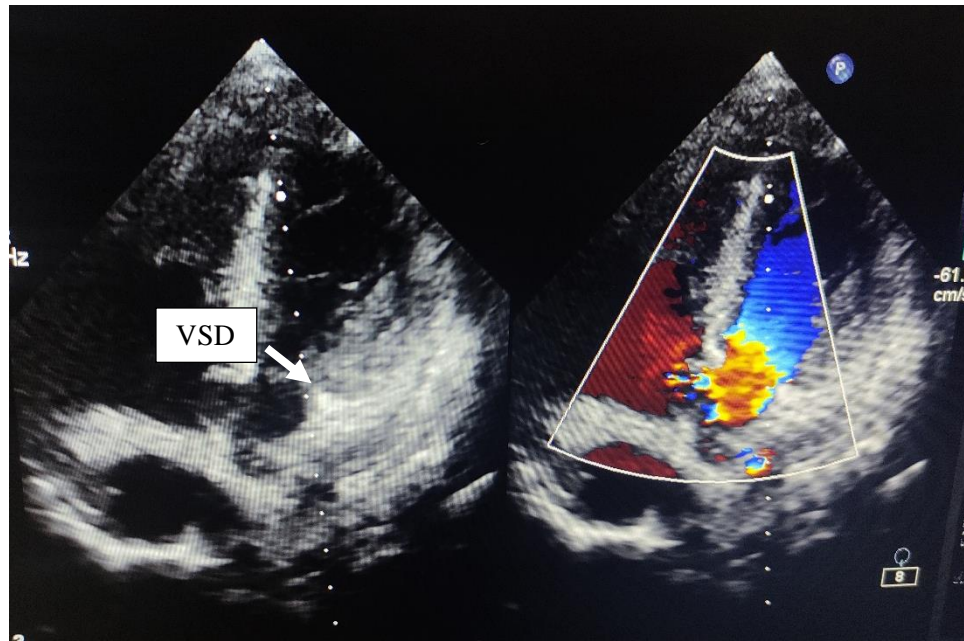


Figure 3 showing ventricular septal defect with left to right shunt on Doppler

3. DISCUSSION

CAKUT was found in 0.5 percent of live births and is a leading cause of kidney failure. The etiological origin is likely multifactorial including chromosomal anomalies, Mendelian inheritance, syndromic, exposure to teratogens, and most likely a genetic-environmental interaction (Calderon-Margalit et al., 2021). CAKUT can manifest as a single ailment or as part of a systemic illness including extrarenal presentations, because the urinary and cardiovascular systems have mesoderm as same embryological origin, an injury to which during period of embryogenesis may affect organs of both systems. According to a research, 29 percent of mutations leading to congenital heart disease (CHD) also induce renal abnormalities in 135 lines of mice found in mutational screening of mice. Patients of CHD were examined for clinical correlation, and discovered a 30% co-occurrence of renal anomalies. These findings contribute to a similar genetic origin for renal and CHD abnormalities, implying an elevated risk of renal anomalies and their consequences in patients with CHD (Rodriguez, 2014).

CAKUT is caused by an alteration of nephrogenesis, which can be due to environmental or genetic factors such as gestational diabetes and use of ACE-inhibitors in intrauterine period. CAKUT malformations on the other hand noticed in family members highlighted the eminence of genetics and drives towards research (Capone et al., 2017). A spectrum of renal-related birth abnormalities can be caused by alteration in the embryological development of kidney. CAKUT encompasses a wide range of anomalies, including pelviureteral junction obstruction (PUJO), multicystic dysplastic kidney (MCDK), renal hypodysplasia, renal agenesis, horse-shoe kidney, ectopic kidney, primary vesicoureteric reflux (VUR), posteriorurethral valve (PUV), and vesicoureteral junctional obstruction (VUJO), and the duplex collecting system (Kumar et al., 2019) (Figure 4a, 4b).

Renal abnormalities can also come about as a consequence of syndromes such VACTERL, renal coloboma (kidneys, eyes), Fraser syndrome (kidneys, genitalia). Furthermore, ciliopathies are commonly coexistent with cystic kidney disease and other organ abnormalities. The genetic involvement in various abnormalities detected were cystic kidney disease having involvement of two genes (PKD1 and PKD2) for dominant and single gene (PKHD1) having the recessive variant of PKD, renal coloboma syndrome identified with Pax2 gene, renal cystic disease and diabetes (Hnf1b) (Atwell et al., 1974).

Barakat et al., (1988) states that; extrarenal anomalies were seen in 47% of CAKUT autopsies and sixty percent below 18 year old children. CV abnormalities are 10 times more common in patients with CAKUT compared to controls. In their study, ventricular septal defect (VSD) accounted for 60% of the CV abnormalities, with atrial septal defect (ASD) and pulmonary stenosis accounting for 25% each. In the autopsy investigation by Barakat et al., (1988) individuals with CAKUT had concomitant cardiac and CV abnormalities in 25% of the cases. Agustin et al., (2016) revealed 30% patients having cardiac association along with CAKUT in his study with various structural anomalies. According to Jiang et al., (2020) 7.4% of children with CHD also have CAKUT. Majority children had hydronephrosis as renal anomaly and atrial septal defect as cardiac anomaly in this study. According to a cohort study made for 30 years on 312 children affected with CAKUT showed poor prognosis and outcome in bilateral renal hypodysplasia, posterior urethral valves and single kidney compared to other anomalies (Caruana & Bertram, 2015).

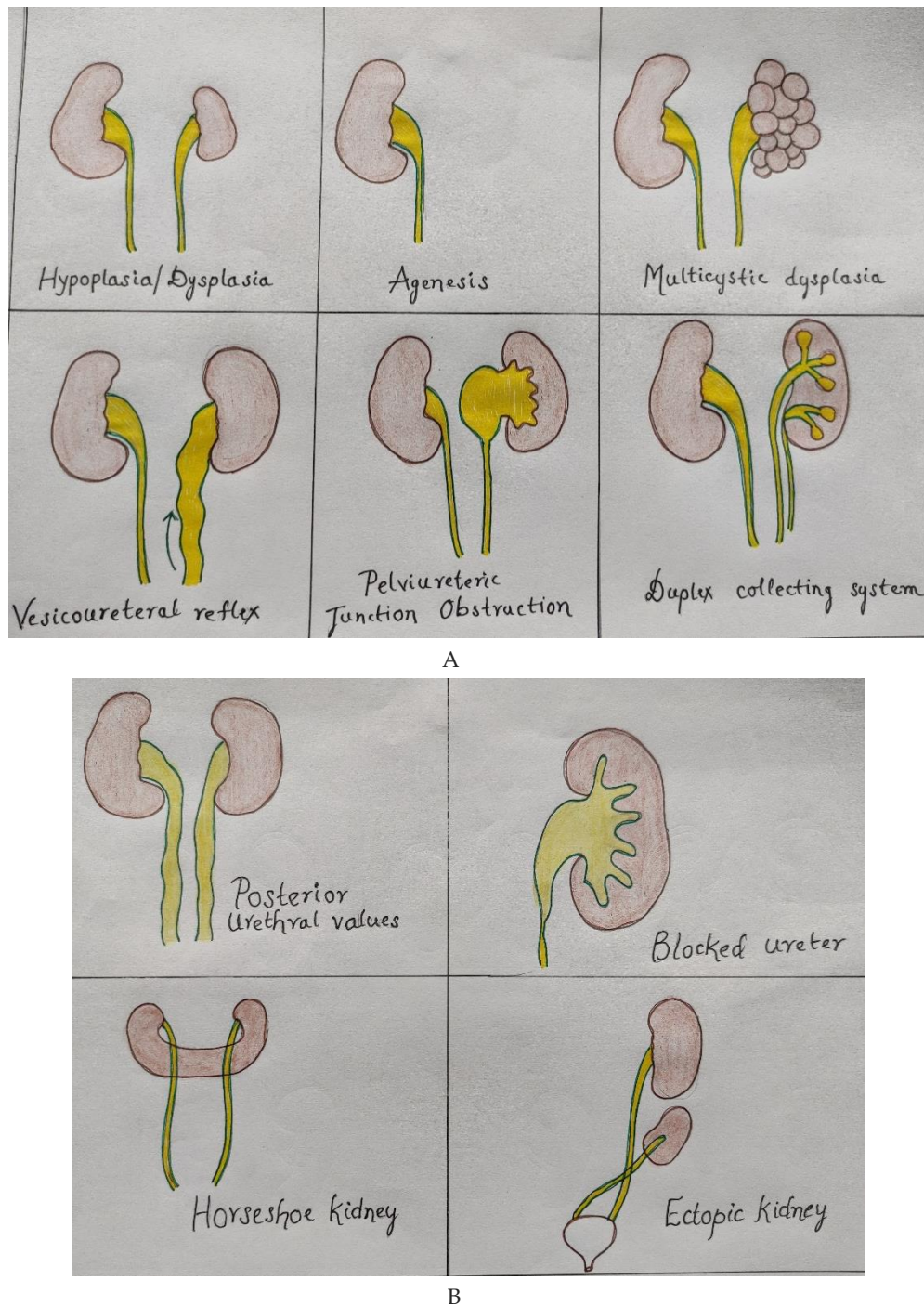


Figure 4 A and B showing various renal anomalies in CAKUT syndrome

In this case patient had unilateral renal hypoplasia on left side along with ventricular septal defect presented with ESRD symptoms. Hence we intervened by initiating hemodialysis and other supportive medical management. Later patient was planned for renal transplantation. Prompt diagnosis is essential in the prevention and timely intervention in these patients. A physician should be alerted to look for CAKUT if there are anomalies in other organ systems. Exploring the many gene mutations the authors have described in individuals with both of these problems, according to the authors, may give distinctive cognizance regarding cardiac and renal malformations. Previous data also aims at extra cardiac problems in CHD mutants and discovered an astonishingly high occurrence of kidney anomalies.

5. CONCLUSION

In conclusion, CAKUT is far more prevalent in CHD patients than it is in the general population. For patients with CHD, ultrasound abdomen is suggested as a regular checkup. Routine assessment of the renal system is essential during the investigative

workup of CHD patients to minimise the risk of renal complications and enhance clinical outcomes. As genetic investigations were not performed in our case, we are unable to give a scientific base for determining the causation of CHD complicated by CAKUT at the gene level. This section of this study requires more investigation. Even though CAKUT is frequently the initial presentation of a complicated systemic illness, an early diagnosis can aid physicians in detecting additional subtle clinical presentations, which can have a substantial impact on patient care and prognosis.

Acknowledgement

We thank all the contributors involved in this study.

Author Contributions

VVSSS and SA had initiated the idea of publication and contributed to the development of manuscript.

SG had performed the echocardiography and diagnosed ventricular septal defect.

RKS had diagnosed renal hypoplasia on CT scan and provided precise images.

SA, SS and SK reviewed and edited the manuscript.

CVSA had provided related information regarding congenital anomalies and drawings of the renal anomalies in CAKUT syndrome.

Informed consent

Written and oral consent was obtained from the participant involved in the study.

Funding

The study did not receive any external funding.

Conflict of interests

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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